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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/975,519	11/20/97	ZHANG	5 INGN:036

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EXAMINER	
MOSHER,M	
ART UNIT	**PAPER NUMBER**
1643	

DATE MAILED: 09/25/98

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

1-File Copy

PTO-90C (REV. 2/95)

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Office Action Summary

Application No.	Applicant(s)
08/975,519	Zhang et al
Examiner	**Group Art Unit**
Mary Mosher	1643

☒ Responsive to communication(s) filed on *5/22/98*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-69* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-58 and 60-69* is/are rejected.

☒ Claim(s) *59* is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *3*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Claim Rejections - 35 USC § 112

Claims 1-42, 61-63, and 69 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "low perfusion rate" in claims 1 and 31 is a relative term which renders the claim indefinite. The term "low" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claims 61-62 lack antecedent basis for "said detergent". Claim 63 lacks antecedent for "said isolating". There is insufficient antecedent basis for this limitation in the claim.

Claim 69 lacks antecedent for "said adaptation for growth", since "adaptation" is a process and parent claim 66 is a product, an adapted cell. Is the intent to claim the cell of claim 66 made by a process of growing cells with sequential decrease in the serum content of the media?

Claim Objections

Claims 53 and 57 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Since claim 52 requires "growing cells in serum-free medium", the cells must necessarily be adapted for growth in serum free medium. Therefore claim

53 provides no further limitation. In addition, claim 57 expands rather than limits the scope of claim 53, since claim 57 permits up to 0.03% serum and claim 53 requires no serum.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 66, 67, and 69 are rejected under 35 U.S.C. 102(a) as being clearly anticipated by Morris et al (C22) and Gilbert (C6).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 31-42, 51, and 65 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Huyge et al (C14). These claims are drawn to an adenovirus, described in product-by-process language. Since the characteristics of an adenovirus are determined by the viral genome, a virus has the same characteristics (or very similar characteristics) regardless of the method used to produce a purified suspension of viruses. Since both applicant's method and the reference method produce purified p53 recombinant adenoviruses, the virus products are seen as identical, or so similar as to be obvious variants. The Patent Office does not have facilities to produce applicant's product-by-process virus and compare it to other, similar prior art products.

Claims 1-16, 21-30, are rejected under 35 U.S.C. 103(a) as being unpatentable over Huyge et al (C14) in view of Perrin et al (C25), Garnier et al (C5), Nadeau et al, and any of Fanget et al, Trepanier et al, or Payment et al. Huyge et al describes a method for producing an adenovirus comprising harvesting and lysing cells, reducing the concentration of contaminating nucleic acids with Benzonase, and isolating the virus with any of a variety of chromatographic media, including anion exchange chromatography. This differs from the claimed invention in that (1) the host cells were grown in batch mode, not perfused during growth, (2) the crude cell lysate was not concentrated and buffer exchanged. However, in the art of virus production, perfusion cultures have been used for large-scale growth of cells for virus production, for example by Perrin et al, and Garnier et al and Nadeau et al teach scale-up of adenovirus growth using medium replacement and fed-batch conditions controlling the glucose concentration for improved yield. It

would have been within the ordinary skill of the art to scale up culture using a perfusion system, for the advantages of large-scale production of virus as suggested by Perrin et al, and to optimize the rate of medium replacement and glucose level for the advantage of improving yield as taught for adenovirus by Garner et al and Nadeau et al. In addition, ultrafiltration and diafiltration methods for concentrating virus and exchanging buffer are known in the art, see for example Fanget et al, Trepanier et al, or Payment et al. It would have been within the ordinary skill of the art to choose a combination of known methods for large-scale virus growth and harvest, and to further perform routine optimization. Therefore, the invention as a whole is seen as prima facie obvious, absent unexpected results.

Claims 17-19, 43-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huyge et al (C14) in view of Perrin et al (C25), Garner et al, Nadeau et al, and any of Fanget et al, Trepanier et al, or Payment et al as applied to claims 1-16, 21-30 above, and further in view of Graham et al (C7). These claims differ from the above in requiring cell lysis using a detergent. Graham et al teaches that 5% sodium deoxycholate can be used to disrupt cells without disrupting adenovirus virions, see page 119. Therefore it would have been obvious to use deoxycholate or another detergent as an alternative method to lyse the infected cells.

Claims 52-58, 60-64 are rejected under 35 U.S.C. 103(a) as being unpatentable over Huyge et al (C14) in view of Perrin et al (C25), Garner et al, Nadeau et al, any of Fanget et al, Trepanier et al, or Payment et al, and Graham et al (C7) as applied to claims 1-19, 21-30, and 43-50 above, and further in view of Morris et al (C22) or Gilbert (C6). These claims differ from the

above in requiring serum-free media. Cells adapted to serum-free medium have been used for large scale production of viruses, see for example Perrin et al, for the purposes of inexpensive scale up. Morris et al and Gilbert specifically teach production of adenovirus in cells adapted to serum-free media. It therefore would have been obvious to further use cells adapted to serum-free media, for the purposes of reduced expense.

Claim 68 is rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Morris et al (C22) or Gilbert (C6). The references teach 293 cells adapted for serum-free medium, which appear to have characteristics the same as, or similar to, the cell line recited in the claim. The patent office does not have the facilities to compare applicant's cell line to prior art cell lines which appear to have the same or very similar characteristics. Therefore the invention as a whole is seen as prima facie obvious over the previously described cell line, if not anticipated.

Conclusion

Claims 20, 59 are seen as free of the art, because the prior art does not teach or suggest harvest of virus after autolysis of adenovirus-infected cells.

Claim 59 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is (703) 308-2926. The

examiner can normally be reached on Monday -Thursday and alternate Fridays from 6:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marian Knode, can be reached on (703) 308-4311. The fax phone number for this Group is now (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196 .

September 23, 1998

MARY E. MOSHER
PRIMARY EXAMINER

MARY E. MOSHER
PRIMARY EXAMINER
GROUP 1600